1

SEQUENCE LISTING

<110> DOWNES, MICHAEL R.
 VERDICIA, MARK A.
 NOEL, JOSEPH P.
 EVANS, RONALD M.
 BOWMAN, LINDSEY J.
 BOWMAN, MARIANNE

<120> STRUCTURE OF THE FARNESOID X RECEPTOR LIGAND BINDING DOMAIN AND METHODS OF USE THEREFOR

<130> SALK3140-1

<140> 10/535,042

<141> 2005-05-13

<150> PCT/US03/036548

<151> 2003-11-14

<150> 60/426,665

<151> 2002-11-15

<150> 60/426,668

<151> 2002-11-15

<160> 6

<170> PatentIn Ver. 3.3

<210> 1

<211> 476

<212> PRT

<213> Homo sapiens

<400> 1

Met Gly Ser Lys Met Asn Leu Ile Glu His Ser His Leu Pro Thr Thr 1 5 10 15

Asp Glu Phe Ser Phe Ser Glu Asn Leu Phe Gly Val Leu Thr Glu Gln 20 25 30

Val Ala Gly Pro Leu Gly Gln Asn Leu Glu Val Glu Pro Tyr Ser Gln 35 40 45

Tyr Ser Asn Val Gln Phe Pro Gln Val Gln Pro Gln Ile Ser Ser Ser 50 55 60

Ser Tyr Tyr Ser Asn Leu Gly Phe Tyr Pro Gln Gln Pro Glu Glu Trp 65 70 75 80

Tyr Ser Pro Gly Ile Tyr Glu Leu Arg Arg Met Pro Ala Glu Thr Leu 85 90 95

Tyr Gln Gly Glu Thr Glu Val Ala Glu Met Pro Val Thr Lys Lys Pro 100 105 110

- Arg Met Gly Ala Ser Ala Gly Arg Ile Lys Gly Asp Glu Leu Cys Val
- Val Cys Gly Asp Arg Ala Ser Gly Tyr His Tyr Asn Ala Leu Thr Cys 130 135 140
- Glu Gly Cys Lys Gly Phe Phe Arg Arg Ser Ile Thr Lys Asn Ala Val 145 150 155 160
- Tyr Lys Cys Lys Asn Gly Gly Asn Cys Val Met Asp Met Tyr Met Arg 165 170 175
- Arg Lys Cys Gln Glu Cys Arg Leu Arg Lys Cys Lys Glu Met Gly Met
 180 185 190
- Leu Ala Glu Cys Met Tyr Thr Gly Leu Leu Thr Glu Ile Gln Cys Lys 195 200 205
- Ser Lys Arg Leu Arg Lys Asn Val Lys Gln His Ala Asp Gln Thr Val 210 215 220
- Asn Glu Asp Ser Glu Gly Arg Asp Leu Arg Gln Val Thr Ser Thr Thr 225 230 235 240
- Lys Ser Cys Arg Glu Lys Thr Glu Leu Thr Pro Asp Gln Gln Thr Leu 245 250 255
- Leu His Phe Ile Met Asp Ser Tyr Asn Lys Gln Arg Met Pro Gln Glu 260 265 270
- Ile Thr Asn Lys Ile Leu Lys Glu Glu Phe Ser Ala Glu Glu Asn Phe 275 280 285
- Leu Ile Leu Thr Glu Met Ala Thr Asn His Val Gln Val Leu Val Glu 290 295 300
- Phe Thr Lys Lys Leu Pro Gly Phe Gln Thr Leu Asp His Glu Asp Gln 305 310 315 320
- Ile Ala Leu Leu Lys Gly Ser Ala Val Glu Ala Met Phe Leu Arg Ser 325 330 335
- Ala Glu Ile Phe Asn Lys Lys Leu Pro Ser Gly His Ser Asp Leu Leu 340 345 350
- Glu Glu Arg Ile Arg Asn Ser Gly Ile Ser Asp Glu Tyr Ile Thr Pro 355 360 365
- Met Phe Ser Phe Tyr Lys Ser Ile Gly Glu Leu Lys Met Thr Gln Glu 370 375 380
- Glu Tyr Ala Leu Leu Thr Ala Ile Val Ile Leu Ser Pro Asp Arg Gln 385 390 395 400
- Tyr Ile Lys Asp Arg Glu Ala Val Glu Lys Leu Gln Glu Pro Leu Leu 405 410 415

Asp Val Leu Gln Lys Leu Cys Lys Ile His Gln Pro Glu Asn Pro Gln 420 425 430

His Phe Ala Cys Leu Leu Gly Arg Leu Thr Glu Leu Arg Thr Phe Asn 435 440

His His His Ala Glu Met Leu Met Ser Trp Arg Val Asn Asp His Lys 450 455 460

Phe Thr Pro Leu Leu Cys Glu Ile Trp Asp Val Gln 465 470 475

<210> 2

<211> 472

<212> PRT

<213> Homo sapiens

<400> 2

Met Gly Ser Lys Met Asn Leu Ile Glu His Ser His Leu Pro Thr Thr 1 5 10 15

Asp Glu Phe Ser Phe Ser Glu Asn Leu Phe Gly Val Leu Thr Glu Gln
20 25 30

Val Ala Gly Pro Leu Gly Gln Asn Leu Glu Val Glu Pro Tyr Ser Gln
35 40 45

Tyr Ser Asn Val Gln Phe Pro Gln Val Gln Pro Gln Ile Ser Ser Ser 50 55 60

Ser Tyr Tyr Ser Asn Leu Gly Phe Tyr Pro Gln Gln Pro Glu Glu Trp
65 70 75 80

Tyr Ser Pro Gly Ile Tyr Glu Leu Arg Arg Met Pro Ala Glu Thr Leu 85 90 95

Tyr Gln Gly Glu Thr Glu Val Ala Glu Met Pro Val Thr Lys Lys Pro

Arg Met Gly Ala Ser Ala Gly Arg Ile Lys Gly Asp Glu Leu Cys Val 115 120 125

Val Cys Gly Asp Arg Ala Ser Gly Tyr His Tyr Asn Ala Leu Thr Cys 130 135 140

Glu Gly Cys Lys Gly Phe Phe Arg Arg Ser Ile Thr Lys Asn Ala Val 145 150 155 160

Tyr Lys Cys Lys Asn Gly Gly Asn Cys Val Met Asp Met Tyr Met Arg 165 170 175

Arg Lys Cys Gln Glu Cys Arg Leu Arg Lys Cys Lys Glu Met Gly Met 180 185 190

Leu Ala Glu Cys Leu Leu Thr Glu Ile Gln Cys Lys Ser Lys Arg Leu 195 200 205 Arg Lys Asn Val Lys Gln His Ala Asp Gln Thr Val Asn Glu Asp Ser 210 220

Glu Gly Arg Asp Leu Arg Gln Val Thr Ser Thr Thr Lys Ser Cys Arg 225 230 235 240

Glu Lys Thr Glu Leu Thr Pro Asp Gln Gln Thr Leu Leu His Phe Ile
245 250 255

Met Asp Ser Tyr Asn Lys Gln Arg Met Pro Gln Glu Ile Thr Asn Lys 260 265 270

Ile Leu Lys Glu Glu Phe Ser Ala Glu Glu Asn Phe Leu Ile Leu Thr 275 280 285

Glu Met Ala Thr Asn His Val Gln Val Leu Val Glu Phe Thr Lys Lys 290 295 300

Leu Pro Gly Phe Gln Thr Leu Asp His Glu Asp Gln Ile Ala Leu Leu 305 310 315 320

Lys Gly Ser Ala Val Glu Ala Met Phe Leu Arg Ser Ala Glu Ile Phe 325 330 335

Asn Lys Lys Leu Pro Ser Gly His Ser Asp Leu Leu Glu Glu Arg Ile 340 345 350

Arg Asn Ser Gly Ile Ser Asp Glu Tyr Ile Thr Pro Met Phe Ser Phe 355 360 365

Tyr Lys Ser Ile Gly Glu Leu Lys Met Thr Gln Glu Glu Tyr Ala Leu 370 375 380

Leu Thr Ala Ile Val Ile Leu Ser Pro Asp Arg Gln Tyr Ile Lys Asp 385 390 395 400

Arg Glu Ala Val Glu Lys Leu Gln Glu Pro Leu Leu Asp Val Leu Gln 405 410 415

Lys Leu Cys Lys Ile His Gln Pro Glu Asn Pro Gln His Phe Ala Cys 420 425 430

Leu Leu Gly Arg Leu Thr Glu Leu Arg Thr Phe Asn His His Ala 435 440 445

Glu Met Leu Met Ser Trp Arg Val Asn Asp His Lys Phe Thr Pro Leu 450 455 460

Leu Cys Glu Ile Trp Asp Val Gln 465 470

<210> 3

<211> 229

<212> PRT

<213> Homo sapiens

<400> 3

Glu Leu Thr Pro Asp Gln Gln Thr Leu Leu His Phe Ile Met Asp Ser 1 5 10 15

Tyr Asn Lys Gln Arg Met Pro Gln Glu Ile Thr Asn Lys Ile Leu Lys 20 25 30

Glu Glu Phe Ser Ala Glu Glu Asn Phe Leu Ile Leu Thr Glu Met Ala 35 40 45

Thr Asn His Val Gln Val Leu Val Glu Phe Thr Lys Lys Leu Pro Gly 50 55 60

Phe Gln Thr Leu Asp His Glu Asp Gln Ile Ala Leu Leu Lys Gly Ser
65 70 75 80

Ala Val Glu Ala Met Phe Leu Arg Ser Ala Glu Ile Phe Asn Lys Lys 85 90 95

Leu Pro Ser Gly His Ser Asp Leu Leu Glu Glu Arg Ile Arg Asn Ser 100 105 110

Gly Ile Ser Asp Glu Tyr Ile Thr Pro Met Phe Ser Phe Tyr Lys Ser 115 120 125

Ile Gly Glu Leu Lys Met Thr Gln Glu Glu Tyr Ala Leu Leu Thr Ala 130 135 140

Ile Val Ile Leu Ser Pro Asp Arg Gln Tyr Ile Lys Asp Arg Glu Ala 145 150 155 160

Val Glu Lys Leu Gln Glu Pro Leu Leu Asp Val Leu Gln Lys Leu Cys 165 170 175

Lys Ile His Gln Pro Glu Asn Pro Gln His Phe Ala Cys Leu Leu Gly 180 185 190

Arg Leu Thr Glu Leu Arg Thr Phe Asn His His His Ala Glu Met Leu 195 200 205

Met Ser Trp Arg Val Asn Asp His Lys Phe Thr Pro Leu Cys Glu 210 215 220

Ile Trp Asp Val Gln 225

<210> 4

<211> 305

<212> PRT

<213> Homo sapiens

<400> 4

Lys Leu Ser Glu Glu Gln Gln Arg Ile Ile Ala Ile Leu Leu Asp Ala 1 5 10 15

His His Lys Thr Tyr Asp Pro Thr Tyr Ser Asp Phe Cys Gln Phe Arg
20 25 30

Pro Pro Val Arg Val Asn Asp Gly Gly Gly Ser His Pro Ser Arg Pro 35 40 45

Asn Ser Arg His Thr Pro Ser Phe Ser Gly Asp Ser Ser Ser Cys
50 55 60

Ser Asp His Cys Ile Thr Ser Ser Asp Met Met Asp Ser Ser Ser Phe 65 70 75 80

Ser Asn Leu Asp Leu Ser Glu Glu Asp Ser Asp Asp Pro Ser Val Thr 85 90 95

Leu Glu Leu Ser Gln Leu Ser Met Leu Pro His Leu Ala Asp Leu Val

Ser Tyr Ser Ile Gln Lys Val Ile Gly Phe Ala Lys Met Ile Pro Gly 115 120 125

Phe Arg Asp Leu Thr Ser Glu Asp Gln Ile Val Leu Leu Lys Ser Ser 130 135 140

Ala Ile Glu Val Ile Met Leu Arg Ser Asn Glu Ser Phe Thr Met Asp 145 150 155 160

Asp Met Ser Trp Thr Cys Gly Asn Gln Asp Tyr Lys Tyr Arg Val Ser 165 170 175

Asp Val Thr Lys Ala Gly His Ser Leu Glu Leu Ile Glu Pro Leu Ile 180 185 190

Lys Phe Gln Val Gly Leu Lys Lys Leu Asn Leu His Glu Glu Glu His 195 200 205

Val Leu Leu Met Ala Ile Cys Ile Val Ser Pro Asp Arg Pro Gly Val 210 215 220

Gln Asp Ala Ala Leu Ile Glu Ala Ile Gln Asp Arg Leu Ser Asn Thr 225 230 235 240

Leu Gln Thr Tyr Ile Arg Cys Arg His Pro Pro Pro Gly Ser His Leu 245 250 255

Leu Tyr Ala Lys Met Ile Gln Lys Leu Ala Asp Leu Arg Ser Leu Asn 260 265 270

Glu Glu His Ser Lys Gln Tyr Arg Cys Leu Ser Phe Gln Pro Glu Cys 275 280 285

Ser Met Lys Leu Thr Pro Leu Val Leu Glu Val Phe Gly Asn Glu Ile 290 295 300

Ser

305

- <210> 5
- <211> 293
- <212> PRT
- <213> Homo sapiens
- <400> 5
- Gly Leu Thr Glu Glu Gln Arg Met Met Ile Arg Glu Leu Met Asp Ala 1 5 10 15
- Gln Met Lys Thr Phe Asp Thr Thr Phe Ser His Phe Lys Asn Phe Arg
 20 25 30
- Leu Pro Gly Val Leu Ser Ser Gly Cys Glu Leu Pro Glu Ser Leu Gln 35 40 45
- Ala Pro Ser Arg Glu Glu Ala Ala Lys Trp Ser Gln Val Arg Lys Asp
 50 55 60
- Leu Cys Ser Leu Lys Val Ser Leu Gln Leu Arg Gly Glu Asp Gly Ser 65 70 75 80
- Val Trp Asn Tyr Lys Pro Pro Ala Asp Ser Gly Gly Lys Glu Ile Phe 85 90 95
- Ser Leu Leu Pro His Met Ala Asp Met Ser Thr Tyr Met Phe Lys Gly
 100 105 110
- Ile Ile Ser Phe Ala Lys Val Ile Ser Tyr Phe Arg Asp Leu Pro Ile 115 120 125
- Glu Asp Gln Ile Ser Leu Leu Lys Gly Ala Ala Phe Glu Leu Cys Gln 130 135 140
- Leu Arg Phe Asn Thr Val Phe Asn Ala Glu Thr Gly Thr Trp Glu Cys 145 150 155 160
- Gly Arg Leu Ser Tyr Cys Leu Glu Asp Thr Ala Gly Gly Phe Gln Gln
 165 170 175
- Leu Leu Glu Pro Met Leu Lys Phe His Tyr Met Leu Lys Lys Leu 180 185 190
- Gln Leu His Glu Glu Glu Tyr Val Leu Met Gln Ala Ile Ser Leu Phe 195 200 205
- Ser Pro Asp Arg Pro Gly Val Leu Gln His Arg Val Val Asp Gln Leu 210 215 220
- Gln Glu Gln Phe Ala Ile Thr Leu Lys Ser Tyr Ile Glu Cys Asn Arg 225 230 235 240
- Pro Gln Pro Ala His Arg Phe Leu Phe Leu Lys Ile Met Ala Met Leu 245 250 255
- Thr Glu Leu Arg Ser Ile Asn Ala Gln His Thr Gln Arg Leu Leu Arg 260 265 270

Ile Gln Asp Ile His Pro Phe Ala Thr Pro Leu Met Gln Glu Leu Phe 275 280 285

Gly Ile Thr Gly Ser 290

<210> 6

<211> 240

<212> PRT

<213> Homo sapiens

<400> 6

Thr Ser Ser Ala Asn Glu Asp Met Pro Val Glu Arg Ile Leu Glu Ala 1 5 10 15

Glu Leu Ala Val Glu Pro Lys Thr Glu Thr Tyr Val Glu Ala Asn Met
20 25 30

Gly Leu Asn Pro Ser Ser Pro Asn Asp Pro Val Thr Asn Ile Cys Gln
35 40 45

Ala Ala Asp Lys Gln Leu Phe Thr Leu Val Glu Trp Ala Lys Arg Ile 50 55 60

Pro His Phe Ser Glu Leu Pro Leu Asp Asp Gln Val Ile Leu Leu Arg 65 70 75 80

Ala Gly Trp Asn Glu Leu Leu Ile Ala Ser Phe Ser His Arg Ser Ile 85 90 95

Ala Val Lys Asp Gly Ile Leu Leu Ala Thr Gly Leu His Val His Arg
100 105 110

Asn Ser Ala His Ser Ala Gly Val Gly Ala Ile Phe Asp Arg Val Leu 115 120 125

Thr Glu Leu Val Ser Lys Met Arg Asp Met Gln Met Asp Lys Thr Glu 130 135 140

Leu Gly Cys Leu Arg Ala Ile Val Leu Phe Asn Pro Asp Ser Lys Gly
145 150 155 160

Leu Ser Asn Pro Ala Glu Val Glu Ala Leu Arg Glu Lys Val Tyr Ala 165 170 175

Ser Leu Glu Ala Tyr Cys Lys His Lys Tyr Pro Glu Gln Pro Gly Arg 180 185 190

Phe Ala Lys Leu Leu Leu Arg Leu Pro Ala Leu Arg Ser Ile Gly Leu 195 200 205

Lys Cys Leu Glu His Leu Phe Phe Phe Lys Leu Ile Gly Asp Thr Pro 210 215 220

Ile Asp Thr Phe Leu Met Glu Met Leu Glu Ala Pro His Gln Met Thr 225 230 235 240